BERNARDS et al. Appl. No. 10/542,024 Attv. Ref.: 620-378

Amendment After Final Rejection

Tuesday, September 2, 2008

AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

Claims 1-4. (Canceled)

5. (Previously Presented) An assay method which includes:

bringing a putative modulator into contact with von Hippel-Lindau tumour suppressor (VHL) – interacting deubiquitinase enzyme 1 (VDU1) and an ubiquitinated VDU1 substrate:

determining the ability of the putative modulator to modulate the stabilisation and/or state of ubiquitination of the substrate by VDU1;

bringing the putative modulator into contact with a test system comprising VDU1 and hypoxia inducible factor-alpha (HIF-a);

determining the effect of the putative modulator on the stability and/or state of ubiquitination of HIF-a.

- (Previously Presented) An assay method according to daim 5 in which the test system further comprises VHL.
- 7. (Previously Presented) An assay method according to claim 5, wherein the test system is a cell.
- 8. (Original) An assay method according to claim 7, wherein the cell is under hypoxic conditions.
- (Original) An assay method according to claim 7, wherein the cell is under normoxic conditions

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10. (Currently Amended) An assay method according to claim 7, wherein the effect of the putative modulator on HIF-α stability is determined by the activity of a

reporter gene including a promoter that comprises a target site recognized by HIF.

 $\underline{\text{wherein said reported gene is selected from firefly luciferase, secreted alkaline}$

phosphatase and green fluorescent protein.

Claims 11-12. (Canceled)

13. (Currently Amended) An assay method according to claim 5, wherein the

putative modulator is brought into contact with the test system, which is a cell under

hypoxic conditions such that the HIF pathway is $\hbox{\tt [[at]]}\underline{\hbox{\tt under}}$ a high level of activation,

wherein the cell does not contain VHL such that [[whereby -]]VDU1 is capable of

Claims 14-36. (Canceled)

stabilising HIF-α, in the absence of the modulator.

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